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DEPARTMENT OF THE ARMY
Fort Detrick
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Bronchiectasis with situs viscerum inversus.

by M. Kartagener and K. Mully

The peculiar triade: Situs inversus, bronchiectasis and polyposis nasi or chronic sinusitis, to which one of us called attention in 1933, has been the subject of numerous publications during the past years. Previous literature has been summarized in 1935 by Kartagener, in 1939 by Hasler and in 1947 by Kartagener and Gruber. In the latter paper 88 cases were counted. Publications which have appeared since, and those overlooked previously, may be tabulated in chronological order as follows:

1937	Casaubon and Derqui (cited after Olsen)	evidently 1 case
1938	Cockayne	1 case (sister situs inversus without BE)
	Tempini	2 cases (one with simultaneous TB)
1939	Cole and Nalls	1 case
	Natvig	2 cases (siblings)
1940	Dannenbaum (Braunschweig)	1 case (personal report)
	H.E. Meyer	1 case (isolated dextrocardia, mother BE)
	Perry and King	1 case (6 observations, of which 5 were already published 1937 by Adams, Churchill)
	G.O. Wood and Blalock	1 case
	W.B. Wood	1 case ("cystic disease" with dextrocardia, no further data)
1944	Richards	1 case
1946	Toscano	1 case (with congenital cardiopathy)
1947	Allende and Langer	2 cases

1947	Lageze and Buffard	2 cases
1948	Aimes	2 cases
	Benda and Huet	1 case
	Hurter	2 cases (third observation already published by Schaich in 1947)
	Kluge	1 case
	Shepard and Stewart	2 cases (siblings !, 1 other case questionable)
	Tapie, Laporte, Pinel and Denard	1 case (sister BE without inversion)
	Weill, Lallemant and Leveque	1 case (brother: repeated bronchitis and agenesia of the frontal sinuses, one sister died of "maladie bleue")
1949	Andrews	1 case
	Assmann	1 case (Fig. 270 in 6th ed. not identical with Fig. 216 in the 4th edition)
	Bonhag	2 cases (plus 1 case of TB with questionable BE)
	Churchill	1 case
	Fornara	2 cases (3 observations, incl. Toscano's case)
	Langer	1 case
	Mounier-Kuhn	1 case (5th obs. in Soulas-Mounier-Kuhn)
	Ochsner, De Bakey and De Camp	3 cases
	Santy, Berard and Galy	1 case
	Schettler and Klink	1 case (with vascular deformity at fundus oculi)
	Souders	2 cases (may possibly include Adams and Ficarra's case, 1947)
1950	Bergstrom, Cook, scanell and Berenberg	2 cases (siblings, 2 other siblings BE without inversion)
	Blixenkrone-Moller	1 case
	Castanier, Vincent, Hadidi, Rosass and Ripoll	2 cases (brothers, simultaneously papillar edema nervus opticus)

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1950	Cohen, Golstein and Hamill	1 case
	Ferreira and Meira	1 case
	Hogg	1 case
	Jedlicka and Levinsky	11 cases (6 with complete triade, including two sisters, 3 with situs inversus and BE without sinusitis, 2 others by personal report)
1951	Chattas and Di Rienzo	2 cases
	Conway	4 cases (1 case with polydactylism both hands, cousin of one case also has situs inversus)
	Fraga Filho, Nery and Maranhao	1 case
	Kaye and Meyer	2 cases (siblings)
	Murray	1 case
	Sas (cited after Bolechowski and Jaroszewski)	1 case
	Zuckermann and Wurtzebach	1 case (probably the oldest observed case, a 63 year old veteran of the First World War)
1952	Dassen and Gotlieb	1 case (second oldest case, 59 year old woman)
	Ferrand, Sarrouy, Pierrou, Armand and Masson	3 cases (including 1 case without certain BE but with "deformations parietales des bronches de troisieme ordre" as "etat preliminaire a une dilatation bronchique vraie")
	Hebel	2 cases (siblings, another sibling BE without inversion, another sibling asthmatic bronchitis. All four with simultaneous thorax deformities. Father: polyposis nasi)
	Karani	2 cases (sisters. Father: chronic bronchitis. One brother with a "weak chest" —not examined— the heart was supposed to have been found "on the wrong side")
	Pellnitz and Heyland	1 case (pyrgocephalus)
	Pykosz (cited after Bolechowski & Jaroszewski)	1 case
1953	Brusa	1 case
	Dickey	5 cases (incl. 2 siblings, 1 partial situs invers)

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1953	Katz, Benzier, Nangeroni and Sussman	1 case
	Laas (Hamburg)	1 case (personal report)
	Negri	1 case
	Nogueira da Silva and Chiaverini (cited after Cosslo and Caul)	2 cases
	Di Rienzo	1 case
	Welento (cited after Bole-chowski and Jaroszewski)	1 case
1954	Katz, Benzier and Nangeroni	3 cases (including two siblings)
1955	Bolechowski and Jaroszew-ski	5 cases (1 other questionable case)
	Fried	11 cases (roentgenogram examinations, "partial and complete pictures of Kartagener's syndrome)
	Lindskog and Hubbell	3 cases
	Luna	1 case (mother and one brother also BE)
	Stutz and Vieten	2 cases (3rd observation is identical with a case of Hurter, according to personal report)
	Taiana, Villegas and Schiepatti	1 case
1956	Finkler	2 cases (another questionable case)
	Schmuckler	1 case

All together there have been reports of at least 216 individual cases of bronchiectasis with situs inversus (including the case to be described herein), considering the probability of some cases again escaping our attention. In the majority of these cases an involvement of the accessory nasal cavities has been observed as a complement of the triade proper. It follows beyond a doubt that simultaneous occurrence of bronchiectasis and situs inversus (and possibly of sinusitis) is not based on coincidence. Especially striking is the fact that

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this anomaly occurs relatively frequently in several members of the same family. Bronchiectasis or a tendency to chronic bronchitis or chronic sinusitis without inversion also has been observed repeatedly among relatives, as have been siblings or ascending relationships with inversion but without involvement of the respiratory organs. The fact that a number of authors were able to report on several pertinent observations as soon as their attention was directed to this "lusus naturae," is worthy of special consideration. These authors have at times correlated the frequency of this combination to the total number of situs inversus cases seen by them, and have reached a remarkable agreement (with the exception of Finkler)(cf. Table 1).

TABLE 1

Author	Year	Frequency of situs inv.	Bronchiectasis with situs inversus absolute	%
Benda	1905	autops.2:10,000—0.02%	-	-
Sherk	1922	10:34,700—0.003%	-	-
Guenther & Kegel	1923-1925	clinical 0.0079% autops. 0.0134—0.08%	-	-
Lewald	1925	clinical (recruits) 1:35,000—0.003% autops.0.02%,roentg.0.07%*	-	-
Mandelstamm and Reinberg	1928	roentg. 0.06%*	-	-
Kartagener&Horlacher	1935	-	7:30	23.3
Adams and Churchill	1937	clin.23:232,112—0.01%	5:23	21.7
Olsen	1943	-	14:85	16.5
Wegelin	1945	autops. 0.022% partial situs inv.0.035%	2:10	20.0
Wayburn	1946	roentg.(flying personnel) 9:77,016—0.012%	-	-
Taussig	1947	clin. 4:120,000—0.003%	-	-

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TABLE 1 (continued)

Author	Year	Frequency of situs inv.	Bronchiectasis with situs inversus absolute	%
Shepard and Stewart	1948	clin.,partly roentg. 13:460,000-0.003%	2:13	15:3
Blegen (perspective)	1949	roentg.0.015% autops.0.016%	-	-
Jedlicka and Levinsky	1950	-	9:46	19.5
Tandos	1950	roentg. (soldiers) in Vietnam 0.03% in North Africa 0.02% in Europe 0.008%		
Nogueira and Chiaverini	1952	-	2:10	20.0
Torgersen	1952	roentg. about 0.01%	about	25.0
Bolechowski and Jaroszewski	1955	EKG 7:66,000-0.012%		
Fried	1955	roentg. about 1:16,000- 0.06%	11:20*	over 50*
Finkler	1956	roentgenograms about 50:250,000-0.02%	2:50	4.0

* not for evaluation, selected material
** Adams and Churchill's data: 0.002%,should be a misprint

A really imposing confirmation of all these observations, which in the final analysis are still quite isolated, is represented by the systematic examination of Norway's extensive X-ray material by Torgersen. Among approximately 2 million roentgenograms, corresponding to about 2/3 of Norway's population, Torgersen found cases of situs inversus with a frequency of approximately 1:10,000, and among these about 25% with bronchiectasis or the complete triade. Exact, absolute figures are not available from Torgersen's paper. It is assumed to deal with about 200 cases of situs inversus and about 50 cases of situs inversus with bronchiectasis, partly with simultaneous sinusitis.

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Similar, but less systematic examinations were conducted by Fried in

Berlin and Finkler in Israel. Their results are shown in the table.

The following are considered questionable, more or less probable cases,

listed in chronological order:

1884 Wehn	clinical: left bronchiectasic cavity, autopsy points to more probable TB (no histologic examination, no bacteriologic evaluation)
1897 Vehsemeyer	first roentgenogram of a case of congenital dextro- ...la upon exposure lasting 13 minutes! (no inversion of abdominal organs, but the right diaphragm is lower; simultaneous chronic pneumonia of the left lung, chronic bronchitis)
1907 Aufdermauer	case 2, total situs inversus,"annoying and long-lasting pulmonary catarrh"
1908 Kehr, Liebold and Neuling	case 194, 55 year old man, bronchitis since childhood, copious sputum in the morning
1932 Cordier and Anstett	emphysema with bronc'ial onsets
1934 Ellman	complete situs inversus, large circular shadow upper left (cyst? cavity? no further data)
1941 Cohen-Tanugi	among 4 cases of situs inversus one case with cough for years, one case with a chronically bronchitic mother.
1948 Shepard and Stewart	case 12 (chronic sinusitis, productive cough, increased pulmonary markings, "suggestive of early bronchiectasis")
1949 Bonhag	1 case with TB and questionable bronchiectasis
Weill	probably identical with the case published in 1948 by Weill, Lallemant and Leveque
1950 Jedlicka and Levinsky	6 cases of situs inversus with relapsing, chronic bronchitis (observations 5,7,25,32,35,42)
1951 Sohier and Boucher	simultaneous generalized Besnier-Boeck-Schaumann with cystic bronchiectasis in the anterior segment of the left superior lobe, diagnosed as postprimary bronchi- ectasis (calcified glands in the left hilus,..o sinusitis)
1952 Karani	see above
1955 Bolechowski and Jaroszewski case 6	
1956 Finkler	case 3

With the exception of the cases of Kartagener and Horlacher (a)(case 1), Kartagener and Gruber, H.E. Meyer, W.B. Wood?, Dickey (case 2) and the questionable case of Vehsemayer, a total inversion of chest and abdominable viscera has always been involved.

Kartagener (a) points to the fact that a left-sided tracheal bronchus, which according to Bigle. was observed only twice before 1924 with situs solitus, was described by Leboucq as early as 1881 in connection with situs inversus. The tracheal bronchus, according to Herxheimer and Gold, is important in genesis of accessory lungs or bronchial cysts, consequently also important for formation of bronchiectasis. In this connection the observation of Holinger, Johnston, Parchet and Zimmermann may be reported: Bilateral tracheal bronchi, which supply both superior lobes, in a 7 month old girl with dextrocardia and several other simultaneous anomalies.

With reference to pathogenesis, the majority of authors agree on the important role of a congenital factor in the appearance of this syndrome. The fact that generally anomalies are quite frequent in connection with situs inversus, that especially in cases of situs inversus with bronchiectasis anomalies are seen also in other organic systems, and particularly the familial occurrence of the triade speaks strongly for the significance of a congenital, possibly a hereditary factor.

Familial occurrence of the triade has been seen 33 times in 15 observations, and this by the following authors: Guenther, Graham, Natvig, Lopez-Areal (4 siblings), Torgersen (2 families with 2 and 3 siblings, respectively), Shepard and Stewart, Bergstroem et al (2 siblings and 2 other siblings with BE without inversion), Castanier et al, Jedlicka and Levinsky, Kaye and Meyer, Hebel (2 siblings and 2 siblings with suspected BE without inversion), Karani (2, perhaps 3 siblings), Dickey, as well as Katz, Benzier and Nangeroni.

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Simultaneous other anomalies are quite frequently noted in the skeletal system: thorax deformities several times, polydactylism (Conway), pyrgocephalus (Pellnitz and Heyland), further, atrophy of the right side of the body (Aimes), Fallot's tetrad (Toscano and Fornara), open septum ventriculorum and transposito vasorum (Dickey), abnormal origin of the left arteria subclavia (Kaye and Meyer), vascular deformity at the fundus oculi (Schettler and Klink), papillary edema (Castanier et al), deafmutism (Kartagener(a), hypoplasia of the genitals and mental underdevelopment (several times).

It is difficult to decide just how this congenital (possibly hereditary) factor influences the genesis of bronchiectasis. In regard to the bronchiectasias one of the following may be involved: A true deformity (congenital bronchiectasis in a narrower sense) or inadequate arrangement (defaut original of Bards) of the supporting apparatus of the bronchial wall (musculature, elastic fibres, cartilage) or a distinct "secretory hyperactivity of the bronchial mucous membrane" (Churchill). The latter possibility is supported by very frequent (but not obligate) involvement of the mucous membrane of the upper air passages noted in early reports of bronchiectasis with situs inversus (Siewert 1904). Mounier Kuhn (cf. also Gregoire) also supposes a "miopragia" of the bronchial and nasal mucous membranes which is congenitally caused, possibly on the basis of hereditary syphilis. Benda and Huet's and Ferrand's et al "predisposition tissulaire" must be interpreted in the same sense. Similar meaning must be ascribed to the questionable or "early" bronchiectasis in the aforementioned cases of Shepard and Stewart, Bolechowski and Jaroszewski, Finkler.

The majority of authors assume -- at least in the cases with situs inversus-- that the alterations in the nasal cavities are coordinated with bronchiectasis (cf. Kartagener and Ulrich). According to Ferrand et al the manifestations in the upper air passages are more intense and precede bronchiectasis considerably.

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In their case 3 sinusitis maxillaris and agenesis of sinus frontalis were present, while the bronchi only showed a "deformation parietale" as a fore-runner of true bronchiectasis. Similar interpretations were made by Benda and Huet, who in their case found sinusitis maxillaris, nasal polyps and absence of frontal sinuses, but only slight bronchiectasis. Considering the age of the patient (7 years), they believe this to be a "borderline case," meaning probably that bronchiectasis has not yet fully developed.

Sohier and Boucher even rejected the congenital nature of bronchiectasis due to absence of sinusitis!

Conversely, sinusitis is caused by bronchiectasis according to Dickey and Hogg. Sinusitis is said to grow out of coughing up of infectious bronchiectasic pus. Hogg was able to prove by X-ray the presence of lipiodol in the sinus maxillaris following bronchography (cf. also Brock).

Direct anatomical proofs of the congenital nature of bronchiectasis are hard to find. So far no related observations of fetuses and newborn are known, which would prove the congenital nature of bronchiectasis by means of its con-nateness. Still, cases of pulmonary cysts or honeycomb-lung in which the congenital moment is probable from the start should be noted here in particular. First the autopsy and biopsy cases: In Wehn's case tubercular cavities seem more likely. Oeri, whose observations were later identified as bronchiectasis by Kartagener, describes "a large cavity" in the left superior lobe. Karta-genen's (a) case 4 (autopsy Prof. Uehlinger) showed generalized bronchiectasis of all pulmonary lobes and honeycomb-lung in the left middle lobe; however, the diagnosis is not quite unequivocal due to secondary tuberculization. According to Ingraham (cited in Zuckerman and Wurtzbach, the original unfortunately was not available to us) the whole picture gave the impression of a "congenital deformity with persistence of peribronchial connective tissue and underdevelop-

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ment of the alveolar structure." The remaining anatomical examiners (cf. especially Oettli and Wegelin) cannot find signs of disturbed development. Findings by Sauerbruch and Lotzing, such as: no important inflammation, complete confusion of elements used in the buildup of bronchial walls, drastically called "pele-mele" by Renault, have not been noted. Dickey's findings will be discussed later.

Clinically, i.e. roentgenologically, pulmonary cysts and honeycomb-lung were noted by:

Perrault ("cystes pulmonaires congenitaux"), Lazeze and Buffard (case 2 "voluminous cystic bronchiectasis" lower left), Weill, Lallemant and Leveque ("enorme poche iuxtacardiaque"), Kluge (walnut-sized circular shadow" upper left), Jedlicka and Levinsky ("cystosis pulmonum") in two sisters), Nagy (honeycombs upper left). Even the uncertain cases of Ellman, Sohier and Boucher (cf. table) may be mentioned here.

The remaining pathologic-anatomical findings do not deviate from those which are usually found with "commonly acquired" bronchiectasias. The same applies to the clinical picture. Anamnestically the leading symptoms, cough and sputum, can be followed into earliest childhood. Characteristically the histories of these cases often show phrases such as: Cough "immediately after birth"(Siewert), the illness is said to have commenced "on the day of birth" (Kartagener (a), or bronchitis "all his life"(Conway), "cough since birth" (Dickey), or "a toujours tousee" (Weill et al). But such information is not less rare in other cases of bronchiectasis, even without inversion. The remaining symptomatology: Copious sputum, mouthfuls of expectorations, possibly hemoptysis and relapsing onsets of fever, is completely identical with that of other bronchiectasias.

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Even roentgenologically and bronchographically speaking, cases of honey-
comb-lung and pulmonary cysts (cf. above) showing the character of congenital-
ness from the start are quite rare. Frequently — 3 in our case — triangular
shadows in the paramediastinal area are reported or depicted as an expression
of atelectasis (cf. Kartagener and Horlacher (b).

Various authors have tried therefore to interpret bronchiectasis, even in
cases with situs inversus, as being the secondary effect of atelectasis, with-
out, however, being able to explain the marked increase in these atelectases,
especially in those cases where a factor of predisposition cannot be denied.
Elsewhere one of us (Kartagener (c) has exhaustively treated the importance of
atelectasis in the genesis of bronchiectasis, considered significant and even
dominating by other authors, especially anglo-saxons (e.g. Lander and Davidson,
Ogilvie, Andrus, Mallory, Perry and King), and has arrived at the following
conclusion: Causally, atelectasis as such is not set above bronchiectasis.
When both changes frequently occur at the same time, they are often coordinated
effects of the common cause: Bronchiostenosis. However, there is a reciprocal
relationship between bronchiostenosis and bronchiectasis, regardless whether
the latter is positioned distally, as is usually the case, or proximally to the
bronchiostenosis, i.e. bronchiostenosis may be the cause as well as the result
of bronchiectasis. A bronchial wall weakened endogenically or exogenically in
its apparatus may lead through collapse of the bronchial wall to collapse of
pulmonary parenchyma (atelectasis, cf. bronchial tuberculosis), similarly an
infected or toxically damaged bronchial mucous membrane may by increased pro-
duction and retention of secretion obturate the bronchial lumen and thereby
cause atelectasis (cf. postoperative atelectasis). Both conditions: The
weakening of the bronchial wall and retention of secretion in the bronchial
lumen are met in every bronchiectasis, regardless of genesis. As it is custo-

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mary since Legendre and Bailley (1844) to consider early childhood bronchiecta-
sis with its accumulation of secretion (due to inadequate respiratory movements
or insufficiently vigorous coughing) a frequent cause of atelectases, the more
the possibility of secondary genesis of atelectases should be evaluated in already
established bronchiectasis.

Aside from other arguments dealt with elsewhere, the frequent findings of
atelectasis in the presently discussed case of bronchiectasis with situs inver-
sus as well as in familial bronchiectasias (a report on which is forthcoming
in this journal), i.e. in bronchiectasias which were generated on the basis of
an idiotypically caused anomaly, is an especially important support of the
assumption of secondary atelectasis founded on already existing bronchiectasis.
The findings of Dickey are particularly illuminating in this connection:

During the autopsy of a 14 months old child (case 1) with the complete
triade we found a defect of the ventricular septum and transposition of the
large vessels with a dilated heart. Right lung collapsed, right principal
bronchus collapsed, without cartilage in the posterior wall.

Fig. 1 a. Sch. A., 21 year old girl, roentgenogram on 13 Nov 1949. Situs
inversus, atelectasis (trianglar shadow) lower left. — Fig. 1 b. Same case.
Exposure on 21 Dec 1954: Status after resection of the left middle and inferior
lobes as well as the right lingula. — Fig. 2. Same case. Bronchogram of the
right lung on 20 Feb 1950. — Fig. 3. Same case. Bronchogram of the left
lung on 27 Feb 1950.

In case 2 (with atelectasis of the left middle lobe) the histologic examin-
ation of the dissected left middle lobe and the inferior segments of the left
superior lobe revealed the "absence of muscular and cartilaginous tissue in
the majority of the peribronchial regions."

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In case 3 (atelectasis of the left middle lobe, lobectomy): "Distinct reduction and destruction of the elastic tissue and smooth musculature in the bronchial wall. Several bronchial cartilages were partially destroyed. The brother of this case (case 4) also was subjected to lobectomy of the atelectasic left middle lobe. Histologic: "Extensive alteration of the pulmonary architecture."

In spite of these marked changes in the bronchial wall, corresponding with Engel's "broncho-malacia" (cf. also Pohl's "tracheo-bronchopathia malacica"), and although within the discussed syndrome "heredity is usually the primary factor or at least the predisposing cause and although it is possible that early development of bronchiectasias is influenced by a developmental shortcoming of the bronchi themselves," Dickey believes that atelectasis precedes bronchiectasis or that bronchiectasis is the result of atelectasis!

A similar role is ascribed to atelectasis by Conway (4 of his own cases, partly with other deformities!), although "a congenital factor may be of importance." On the other hand, Richards rejects the causal importance of roentgenologically proved collapse to the origin of bronchiectasias precisely because of the absence of the other two components of the triade, although in his case the possibility of a postprimary collapse is evident (cf. also Lageze and Buffard).

Blixenkrone-Moller, too, unequivocally favors the secondary nature of atelectasis. In his case the X-ray revealed a basal triangular shadow on the right, representing atelectasis of the right inferior lobe. Bronchoscopic: Mucus in the right bronchus, no compression, no obturation. Lobectomy: No interthoracic adhesions, no middle lobe, no glands, bronchi not compressed, right inferior lobe airless, cylindric dilatation of all bronchi. Histology: Dilatation, especially of the respiratory bronchioles, leukocytes and eosino-

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phils in the lumen. Epithelium highly cylindrical, cilia preserved in places, copious lymph follicles in the bronchial wall, resembling an appendix. Alveoli atelectasic, or filled with serum and erythrocytes, no pneumonia, no old blood pigment. The findings are interpreted by Blixenkrone-Moller as congenital, the pulmonary collapse as secondary.

Fig. 4. Same case: Picture of the accessory nasal cavities on 11 Feb 1950: Antra of Highmore are light, frontal sinuses large. --- Fig. 5. Same case. Solid epithelial cords surrounding bronchiectases (280 X).

We may be permitted to point out the similarity to the findings of Whitwell in connection with what he calls follicular bronchiectasis, in which obturation of the bronchi is found distal to bronchiectasis, however.

Compared to the relatively large amount of material dealing with clinical observations, as listed in the table, the autopsic and especially the biopsic material is quite scanty. Since biopsic findings are superior to autopsic ones in pathogenic clarification of bronchiectasias, we believe to be justified in reporting the following case, which was approached 3 times operatively and which offers other interesting pathogenetic aspects.

Own observation (cited by A. Brunner and Wegmann, The second case of bronchiectasis with situs inversus reported by these authors is identical with the case published by Wernli-Haessig, 1937):

Sch. A., girl, born 1928: First admission to the surgical clinic on 7 Feb 1950. Anamnesis: Parents (not related by blood) and 2 brothers heals y, no pulmonary diseases in the family. As a child had measles, mumps, whooping cough, pneumonia twice. In 1942 angina followed by nephritis. In 1948 appendectomy.

Since childhood persistent cough and copious sputum, evening temperatures, fatigue, no hemoptysis, never TB bacilli. In 1949 the Thurgau-Schaffhaus Sana-

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torium at Davos diagnosed bilateral bronchiectasis. The patient is referred for lobectomy.

Findings: Good nutritional condition, paleness, no clubbed fingers. Clinically and roentgenologically situs viscerum inversus totalis. Typical EKG. Plentiful rales over both lungs. Sputum 40-60 cm^3 daily, purulent, at times fetid, without tubercle bacilli, without elastic fibers.

Thorax X-ray (Fig. 1): Hilar markings not increased, distinct paracardiac triangular shadow lower left (corresponding to atelectasis of the left inferior lobe or a segment of the inferior lobe.) Coronary waist filled on the right, possibly as a result of lingular atelectasis.

Bronchography (Fig. 2 and 3, oblique exposures) reveals marked bronchiectasis in both lingular segments on the right. Left lung (Fig 3) bronchiectasis in the region of the inferior and middle lobes.

The rhinologic examination at the Otolaryngologic Polyclinic (Prof. Ruedli) gave no evidence of sinusitis, no polyposis nasi. On the X-ray film (Fig. 4) the accessory nasal cavities are light, the frontal sinuses large.

On 8 Mar 1950 lobectomy of the left middle lobe and resection of the lower segments of the right inferior lobe were accomplished (Prof. A. Brunner). No significant malformations in the pleura. Basal segments of the left inferior lobe as well as the middle lobe are quite extensively atelectasic. Resection of the basal segment of the inferior lobe, closure of the bronchial stump. Extirpation of the left middle lobe. Coverage of bronchial stumps with a pedunculated flap of the pleura parietalis.

The apical segment of the left inferior lobe is twice the size of a fist and almost completely fills the cavity in the inferior lobar area. Rubber tube to the pleural cavity, instillation of penicillin, stratified closure of the wound. In the dorsal position Monaldi's catheter in the first IKR in front.

Postoperative progress without complications (penicillin aerosol).

The histologic examination of the resectional preparation resulted in the following findings: Fairly well developed pulmonary tissue with numerous cylindrical, saccular and fossulate bronchi. The bronchiectasis in the majority is without cartilages. The bronchial walls are strongly reinforced and the mucous membrance considerably folded. The epithelial lining consists primarily of single or multiple layers of ciliated epithelium, partly of multiple layers of pavement epithelium. The tunica propria is strongly thickened, vascularized almost angiomatously, and showing dense lymphoplasmacellular infiltration, partly with follicular accumulation. The tunica propria is outwardly connected to the muscular layer, which is settled by radial vascular loops. The muscular layer, without sharp demarcation, leads into a covering layer with collapsed alveoli. These are lined largely with a single layer of pavement epithelium. Sporadically, larger solid epithelial buds are found, surrounded by connective tissue with lymphoplasmacellular infiltration (Fig. 5). The interlobular septa show a slightly edematous loosening. The vessels do not show marked intimal thickening.

On 24 Nov 1950 a right lingulectomy was effected (Prof. Brunner). The pleura was free. Lingula slightly larger than a thumb, brown-red (Fig. 6). Remaining lung a pale pink, inflates very nicely. Ligature of arteriae and venae, clamping and severance of the bronchus. Provision of the slightly over 1 c. long bronchial stump. Coverage with a freely transplanted pleural flap, stratified closure of the wound.

Fig. 6. Same case. Dissected lingula. —— Fig. 7. Same case. Cut through the lingula: Numerous irregularly formed tongues of cartilage, plentiful mucous glands. Mucous membrane thickened, folded.

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The histologic examination of the dissected lingula (Fig. 7) reveals numerous bronchiectases in immediate proximity. The tongues of cartilage are irregularly formed, partly at angles to each other, slightly bent, unequally thick. The mucous membrane is thickened and folded everywhere. For the most part it carries a multi-row, single layer ciliated epithelium, seldom multi-layer, single row. No pavement epithelium can be found. Between epithelium and tongues of cartilage and between the individual tongues there are massive deposits of mucus glands.

Postoperative progress was satisfactory in the sense that a distinct decrease in the amount of sputum occurred. Coughing persisted, however, as did the secretion of yellowish-green, rather foamy sputum.

A control bronchography on 8 Nov 1954 (Fig. 8 and 9) revealed unmistakable bronchiectases in the apical segment of the left inferior lobe.

On 2 Dec 1954 segmental resection of the remaining apical segment of the left inferior lobe was accomplished (Mully). The lung was completely fused with the parietal pleura, the apical segment of the inferior lobe was not atelectasic, saccular bronchiectases were well palpable. The segment was severed. The vessels were found in the interlobar fissure, they were callously fused with lymphatic glands. The bronchi were severed peripherically and the segment removed, the the apical segmental bronchus leading to the trunk was found, isolated, severed and closed after Klinkenbergh. Coverage with mediastinal pleura and lymphatic glands. Superior lobe emphysematous, fills the entire pleura. Vena azygos is situated on the left, no anomalies of the heart and the pericardium. Bronchial arteries enlarged but not pathologically changed.

The dissected, fixed resectional preparation can be seen in Fig. 10. Above all it shows 3 strongly distended bronchi with greyish-white surrounding mantles of tissue, in places up to 1-2 mm thick.

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Histologically speaking, the distention in the peripheric bronchial sections also amounts to many times that of the norm. Thus the corresponding pulmonary arteries are about 1/20 narrower than the bronchi. The epithelium generally consists of a multi-row ciliated epithelium. The cilia can still be recognized. The epithelium, however, is rather strongly permeated by lymphocytes and plasma cells, in part also by polynuclear leukocytes with short gaps in the epithelial cover.

In close proximity there are broad mantles of tissue, which are densely infiltrated by lymphocytes. Centers of reaction are distinctly recognizable (cf. Fig. 11). But here, too, infiltrations by polynuclear lymphocytes are seen in places. Finally there follow cuffs of connective tissue, radiating like fingers into the bordering pulmonary tissue. The latter has alternatively wide alveoli, septa usually narrow. But here, too, small star-shaped scars appear.

Fig. 8. Same case. Bronchogram of the apical segment of the left inferior lobe on 8 Nov 1954. --- Fig. 9. The same, oblique exposure. --- Fig. 10. Same case. apical segment of the left inferior lobe, fixed and dissected.

Mantles of connective tissue are especially distinct in the medium-sized bronchi. On the other hand, infiltrations of lymphocytes decrease. Here the epithelium shows distinct metaplasia of pavement cells (cf. Fig. 12). Cartilages are rare, muscle fibers also are quite scanty. The elastic fibers are severely splintered and preserved only in small bunches or in the form of islands (cf. Fig. 13). The larger bronchi still show a distinct ciliated epithelium. Cartilages are well recognizable here, but slightly separated. Bundles of muscle fibers are also distinct. The elastic fiber system is rather meagre (cf. Fig. 13).

Further postoperative progress was satisfactory in every way. The thorax X-ray film on 21 Dec 1954 (Fig. 1 b) still shows a small residual effusion in the left sinus. The left superior lobe is well inflated and fills the entire pleural cavity.

In short summary, the medical history of our patient, 22 years old at the time of first admission, reveals the classic symptomatology of bronchiectasis: Cough and sputum since childhood, subfebrile temperatures of long duration, two pneumonic attacks as well as "traditional pneumopathies" (Marquezy and Renault) in the anamnesis. Frank broncho-blennorrhea. Acoustics: Expansive bilateral bronchitic syndrome. Bronchography revealed bronchiectases (Fig. 2 and 3); on the right side a diffuse distension of the superior and inferior lingular segment, no certain bronchiectasis in the inferior lobe, on the left side diffuse, cylindrical bronchiectases in the left inferior and middle lobes with moderate shrinkage of the inferior and middle lobes. The superior lobar bronchi rather stretched out. In addition situs viscerum inversus totalis. However, the triade is incomplete due to the absence of involvement of the accessory nasal cavities. Frontal sinuses and processi mastoidei are well pneumatized. Further, on the negative side, the absence of clubbed fingers is remarkable.

Within $4\frac{1}{2}$ years the patient is three times subjected to thoracotomy: In the first operation on 8 Mar 1950 the left middle lobe and the lower segment of the left inferior lobe are dissected, on 13 Nov 1950 right lingulectomy is effected, in the third operation on 2 Dec 1954, i.e. at age 26, resection of the left apical inferior lobar segment is accomplished.

Histologic examination of the extirpated lobes and segments revealed no direct evidence in favor of congenitalness, nor did it support the acquired nature of bronchiectasis; in particular, no intra, endo or exo-bronchial

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causes of roentgenologically and biopsically diagnosed atelectasis could be determined. Only the increased and irregularly ordered cartilaginous plates, and possibly the uncommonly numerous mucus glands in Fig. 7 could be admitted to a certain degree as an expression of "dysembryoplasia." On the other hand, the proliferations of the epithelium (Fig. 5), which for Garnier is a sign of the congenital origin of bronchiectasis, should not be evaluated in this sense. They are of frequent occurrence in inflammatory changes of different genesis in various parenchymatous organs (cf. Oudendal, Pagel, Planchu, Policard and Galy), F. Muller has mentioned them in connection with bronchiectasis as early as 1907.

On the other hand, the severe inflammatory alterations connected with bronchiectasias should not be interpreted to mean that the inflammation is the cause and the dilatation its result. Even assuredly congenital, connatally occurring bronchiectasias will quite naturally be infected in the course of life or — as put by Debre and Gilbrin — will disinfect themselves with great difficulty and will reveal correspondingly severe inflammatory changes.

Fig. 11. Same case. Apical segment of the left inferior lobe, dense infiltration by lymphocytes with follicular accumulation and centers of reaction in the tunica propria. --- Fig. 12. Same case. Metaplasia of pavement cells in bronchiectasis. --- Fig. 13. Same case. Elastica stain.

Special attention is due in our case to the bronchiectases in the apical segment of the left inferior lobe, which made the third operation necessary. We believe ourselves justified in assuming, on the basis of the first bronchography and especially on the basis of the histologic changes in the preparation of the last (third) resection, that the bronchiectases were already present at the time of the first hospitalization of the patient. Nevertheless the question of postoperative development of bronchiectases in previously healthy bronchi must be aired. Unequivocal observations of this type have been made several

times (cf. among others Brunner, Mully, Crellin, Lehman, Macon and Curry).
Even in cases with situs inversus, postoperative bronchiectases in segments and
lobes previously proved healthy by means of bronchography have been reported by
Di Rienzo: The left middle lobe of a 15 year old girl with a complete triade
was dissected because of bronchiectasis. The other bronchi, "very closely
studied," were normal. A few months later "bronchiectases of the alveolo-
agenetic type, which generally are considered congenital" were found in the
right inferior lobe and the lingula. In the right inferior region a paracardial,
triangular shadow had appeared. According to Di Rienzo these findings proved
that the bronchiectases, "which accompany inversion of the thoracal viscera,
can regenerate themselves within a short time during life, and that the genesis
of bronchiectasias is associated with a bronchial functional syndrome. Stutz
and Vieten interpret these findings of Di Rienzo as well as their own observa-
tions of minor bronchiectasis in the left inferior lobe, which "obviously had
developed only in childhood," in a 14 year old boy with situs inversus and
polyposis nasi, as idiopathic bronchiectasis in the sense of Bard. Without
mentioning Bard, Wegelin also believes in a "morphologically indeterminable
disposition." In a quite general way postoperatively diagnosed bronchiectasias
remind of Policard and Galy's "bronchiectasies en puissance." Recently Cooley,
Ginsberg, Olsen, Kirklin and Clagett tried to explain the frequency of post-
operative bronchiectasis in children (16.6%!) by the fact that development of
the lung and withit, of bronchiectasis, is not yet completed in childhood.

Since to our knowledge bronchiectasis has not been proved in newborn with
situs inversus, and no anatomical findings (with the possible exception of the
observations of Ingraham) on the roentgenologically diagnosed development of
cysts and honeycombs in situs inversus intra vitam are available, the conse-
quential result of the examinations, even the anatomical ones, is this:

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It is impossible to differentiate bronchiectasis with situs inversus from "common" bronchiectasis found in the autopsic and biopsic material. Taiana, Villegas and Schiepatti also stress the curious fact that pathologic-anatomical findings of the resection specimen in their case could not be differentiated from those of "common bronchiectasis of the acquired type."

And yet one cannot doubt an endogenically or idiotypically caused predisposition to bronchiectasis on the basis of extra-pulmonary findings: Situs inversus, involvement of the accessory nasal cavities, frequent simultaneous deformities and conspicuous familial occurrence. From this factor of predisposition ("defaut original" or "malformation en puissance" of Bard) during the course of life, gradually but irresistably, the disease of bronchiectasis itself may develop without intervention of an inflammatory or mechanical cause (idiopathic bronchiectasis Bard). In other cases (Churchill, Ferrand et al) the development of bronchiectasis must be ascribed to an inflammatory-infectious genesis, similar to the origin of inflammations of the accessory nasal cavities. However, a constitutional anomaly must be held responsible for the persistence and the progression of the inflammation. Olsen, too, presupposes a "deformity of the bronchial trunk as a prime factor" and a release by exogenic moments (obturation, atelectasis and bronchial infection), consequently "congenital and acquired components" of bronchiectasis in his 14 cases of bronchiectasis with situs inversus. Likewise Karani speaks of a congenital defect of the bronchial wall, "perhaps aided by chronic infection." This form of bronchiectasis Kartagener (c) calls "bronchiectasias of mixed etiology" or, paraphrasing an expression of Volhards, endogenically caused, exogenically effected bronchiectasias.

All three possibilities of not acquired bronchiectasis: Congenital bronchiectasis in the proper sense, idiopathic bronchiectasis (Bard) and bronchiectasis

of mixed etiology consequently are realized in bronchiectasias with situs inversus. No anatomical verification exists as yet for the first form. The two last mentioned forms (idiopathic and bronchiectasis of mixed etiology), while they cannot be differentiated from acquired bronchiectasias either clinically, roentgenologically, bronchographically or anatomically, must nevertheless be postulated, on the ground discussed above in detail. This point of view, which shifts its center of gravity to extrapulmonary and even extra-individual considerations, shows many cases of seemingly acquired bronchiectasis, even with situs solitus, in an entirely new light. The pathogenetic relativity of atelectasis, genuine bronchial stenosis, and bronchiectasis, as well as their possible reciprocity are especially illuminated thereby.

SUMMARY

Detailed description of a case of bronchiectasis and situs inversus with reference to the complete bibliography and discussion of the pathogeny of the triade of Kartagener.